Clopidogrel (Plavix®) Criteria for Use in Veteran Patients

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

The following recommendations are based on current medical evidence. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician, however, must make the ultimate judgment regarding the propriety of any course of treatment in light of individual patient situations.

The following document briefly outlines recommendations for clopidogrel for various indications and clinical situations, as outlined below. These are not meant to be all inclusive. For other clinical situations and for those with insufficient evidence to determine risk and benefit, consultation with local experts is advised.

Recommendations for use of clopidogrel post percutaneous coronary intervention (PCI)/stent[1,5, 22-33]

- Patients who receive coronary stents will require dual anti-platelet therapy with aspirin and clopidogrel in order to maintain patency of the artery.
- Clopidogrel should be initiated at the time of the procedure, if not before and ideally continued for 12 months. American Heart Association (AHA) guidelines indicate clopidogrel duration should be guided by stent type [bare metal 1 month, sirolimus (Cypher(r), Cordis) 3 months and paclitaxel (Taxus(r), Boston Scientific) 6 months]. (Level A)
- There is recent evidence that drug eluting stents (DES) may confer a rare but increased risk of late stent thrombosis in certain patient populations (including left main DES, DES of bifurcations, overlapping DES, prior history of late stent thrombosis, and DES of bypass graft), suggesting a longer duration of dual therapy may be needed. The exact duration of clopidogrel therapy in these situations has not been conclusively established, however when making this determination providers must weigh the benefit of prolonged or indefinite clopidogrel therapy against the risk for bleeding on a patient by patient basis. (Level C)[22-32]
- Data emerging from pooled meta-analyses and registries suggest the need for uninterrupted dual antiplatelet therapy (aspirin 325 mg, clopidogrel 75 mg daily) throughout the post-stenting treatment period. Any elective procedures which would require stopping or interrupting this therapy (dental work, colonoscopy, etc.) should be delayed until the minimum treatment duration based on stent type is completed.[33]
- The dose of aspirin following a PCI/stent is 325mg daily. This higher dose of aspirin should be given for one month following bare metal stents, 3 months following sirolimus (Cypher(r), Cordis) stenting, and 6 months post paclitaxel (Taxus(r), Boston Scientific) stents, after which aspirin should be continued indefinitely at a dose of 75 to 162 mg daily.
- Patients undergoing brachytherapy should receive clopidogrel 75 mg and aspirin 325 mg daily for an indefinite period unless there is a bleeding risk. (Level C)

Recommendations for use of clopidogrel in NSTEMI/Unstable angina acute coronary syndromes[1,3,5,6,9,11,13]

- In patients with acute coronary syndrome and /or unstable angina in whom no revascularization procedure is planned, clopidogrel should be added to aspirin as soon as possible for at least 1 month (Level A) and up to 12 months (Level B).
- Clopidogrel will be discontinued after 12 months unless compelling clinical reasons exist to maintain therapy for a longer period (Refer to the section on PCI/Stent for specific guidance on drug eluting stents {DES}).

Recommendations for use of clopidogrel in STEMI acute coronary syndrome[18-20]

- In patients with STEMI < 75 years of age receiving fibrinolytics clopidogrel should be administered as a 300mg loading dose followed by 75mg once daily until hospital discharge (up to 8 days) or longer if undergoing angiography/coronary intervention as described below in recommendations post PCI/Stent. (Level A)
- In patients of any age with STEMI regardless of whether fibrinolytics are utilized clopidogrel should be administered at a dose of 75mg once daily until hospital discharge or up to 4 weeks or longer if undergoing angiography/coronary intervention as described below in recommendations post PCI/Stent. (Level A)
- In patients with STEMI who do not undergo PCI consideration can be given to continuing clopidogrel 75mg once daily for up to 1-year based on extrapolation from trials in NSTEMI/Unstable angina. (Level B)

Recommendations for use of clopidogrel in stable coronary artery disease (CAD)[17]

- There is insufficient evidence to recommend initiation in those patients with stable CAD and who do not meet criteria in this document.
- It is recommended that clopidogrel not be added to aspirin therapy for stable/asymptomatic atherosclerosis and/or for patients with multiple cardiovascular risks unless there are other criteria that have been met. (Level A)

Recommendations for use of clopidogrel in aspirin adverse events[16]

- Clopidogrel should be used in patients who are aspirin allergic, i.e.; anaphylaxis, aspirin induced bronchospasm. (Level A)
- In patients with a history of gastrointestinal complications from aspirin (i.e.; bleeding, stomach upset), adding a proton pump inhibitor to aspirin therapy is preferred over switching to clopidogrel. (Level B)

Recommendations for use of clopidogrel for Coronary Artery Bypass Grafting (CABG)[1,14]

- In patients receiving clopidogrel for ACS, discontinuation is suggested 3-5 days prior to elective CABG. (Level B) and restarted as soon as patient's clinical condition tolerates for up to 12 months**.**
- For those patients undergoing saphenous vein bypass graft and allergic to aspirin, clopidogrel, 300mg, as a loading dose 6 hours after the operation followed by 75mg daily may be initiated. (Level B).
- Clopidogrel may be continued for 1-3 months post CABG. (Level C)

Recommendations for the use of clopidogrel in Peripheral Vascular Disease (PVD)[2,4,12]

- Clopidogrel is not recommended for PVD except in cases of aspirin allergy. (Level B)

Recommendations for the use of clopidogrel in recurrent cerebral ischemic events[7,10,21]

- Patients with recurrence of cerebral ischemic events while on therapy with aspirin should be changed to extended release dipyridamole/aspirin. (Level B)
- Clopidogrel is an alternative for those patients who have had recurrent cerebrovascular events, who have a documented aspirin allergy, as mentioned above or are intolerant of extended release dipyridamole (recurrent headache). (Level B)
- The combination of aspirin and clopidogrel is not advised for secondary stroke prophylaxis due to increased risk of adverse events demonstrated in the MATCH trial. (Level B)

Recommendations for the use of clopidogrel in noncardiac stenting[15]

- Patients who undergo carotid artery stenting may be initiated on clopidogrel 75 mg/day and continued for 4-6 weeks post stent. (Level B)
- Patients who undergo intracranial stents may require longer durations of therapy and can be continued up to 1 year. (Level B)
- Patients who undergo renal artery stenting may be initiated on clopidogrel 75 mg daily for up to 12 months post intervention. (Level I)
- Patients who undergo other peripheral stents (inguinal, popliteal, etc) may be continued on clopidogrel 75 mg daily for 30 days post intervention. (Level C)

Recommendation Grading

A	A strong recommendation that the intervention is always indicated and acceptable
B	A recommendation that the intervention may be useful/effective
C	A recommendation that the intervention may be considered
D	A Recommend that a procedure may be considered not useful / effective, or may be harmful.
I	Insufficient evidence to recommend for or against – the clinician will use their clinical judgment

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Criteria Checklist for Clopidogrel

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Indication for therapy	***Response***
Patient with one of the following conditions: ❑ unstable angina ❑ Acute coronary syndrome(NSTEMI or STEMI) ❑ Post PCI/stent placement ❑ Documented aspirin allergy requiring antiplatelet therapy ❑ Intracranial/carotid stent ❑ Brachytherapy ❑ Peripheral stent (renal, inguinal, popliteal) ❑ Cerebrovascular disease with recurrent ischemia	❑ yes ❑ no ***If no, patient is ineligible to receive clopidogrel***
Duration of therapy	
❑ 1 month-post stent placement ❑ 3 months- post ACS ❑ 9 months- high risk post ACS ❑ 12 month- post stent placement ❑ indefinite- aspirin allergic patient ❑ peripheral stent duration_____ months ❑ other _____	
Dosing	
❑ ACS- 300 mg load orally then daily dose of 75 mg ❑ ACS-600 mg load orally than daily dose of 75 mg ❑ Post stent placement-300 mg load orally then daily dose of 75 mg ❑ Non acute conditions- 75 mg daily	
Monitoring	
❑ Out-patients should have a cardiology referral for indefinite ACS use or longer than 3 month occurrence of ACS ❑ Patients with cerebrovascular disease should have a neurology referral if clopidogrel and aspirin are used together ❑ Patients should be followed for development of neutropenia or thrombotic thrombocytopenic purpura	
Contraindications	
Any of the following: ❑ Active bleeding ❑ History of bleeding diathesis ❑ Known hypersensitivity to clopidogrel or any component of the product	❑ yes ❑ no ***If yes, patient is ineligible to receive clopidogrel***